

REMARKS

**Interview Summary**

Undersigned counsel for Applicants thanks Examiner Singh for extending the courtesy of a personal interview on January 8, 2008. During the Interview, “more specific physical limitation[s] or condition[s],” as requested by the Examiner in the outstanding Office Action, were discussed. Though no agreement *per se* was reached, the Examiner agreed that recitation of a density and/or media composition (*i.e.*, the amendments submitted herewith) would be reviewed favorably.

**Status of the claims**

Claims 1-28 and 88-100 were pending and under active consideration in the subject application. With this submission, claims 1, 11, 12, 13, 15, 27, 93 and 94 have been amended; and claims 4, 92 and 97 have been canceled. No claims have been newly added. Therefore, upon entry of this paper, claims 1-3, 5-28, 88-91, 93-96, and 98-100 will be pending and under active consideration.

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

**Claim rejections under 35 U.S.C. § 102**

Claims 1-7, 9-13, 15-21, 26 and 27 remain provisionally rejected under 35 U.S.C. §102(e) as being allegedly anticipated by copending application no. 09/764,359 (“the ‘359 application”). The Examiner alleges that the copending application teaches “the use of percoll gradients for separation of cell populations for liver.” Without acquiescing to the propriety of the rejection, and solely in the interest of speeding prosecution of the instant application, Applicants have amended the claims to recite media “comprising 25% (w/v) iodixanol,” which cannot be

deemed to encompass standard Percoll-based gradients.<sup>1</sup> Hence, Applicants respectfully submit the pending claims are not anticipated by the cited art. Withdrawal of the subject rejection is respectfully requested.

Claims 1-2 and 6 stand rejected under 35 U.S.C. §102(b) as allegedly anticipated by EP 682106 to Tateno, *et al.* (“Tateno”). The Examiner alleges that the instant method claims do not exclude a standard Percoll-based isolation method and notes that Tateno teaches an isolation method based on Percoll. Again, without acquiescing to the propriety of the rejection, Applicants have amended the claims to recite media “comprising 25% (w/v) iodixanol,” which cannot be deemed to encompass standard Percoll-based gradients. Hence, Applicants respectfully submit the pending claims are not anticipated by the cited art.

### **Claim rejections under 35 U.S.C. § 103**

Claims 1-10, 12-17 and 26 remain rejected under 35 U.S.C. §103(a) as being obvious over Tateno, Singh *et al.*, Acta Physiol Scand 117(4):497-505, April 1983 (“Singh”), and USP No. 5785964 to Naughton *et al.* (“Naughton); claims 1-6, 8, 11-17, 22-28 and 88-100 are rejected under the subject statute as being unpatentable over Tateno, Brill *et al.*, Proc Soc Exp Biol Med. 1993;204(3): 261-9 (“Brill”), Cassiman *et al.* Am J Pathol. 1999;155(6): 1831-9 (“Cassiman”), and Graham, Scientific World J 2:1347-50, May 2002 (“Graham”); claims 1-17, 22-28, 88-100 remain rejected over Tateno, Brill, Cassiman, Graham and Naughton; and claims 1-28 and 88-100 stand rejected as being unpatentable over Tateno, Brill, Cassiman, Graham, Naughton and further in view of US 6,140123 to Dementrious, *et al.* The reasons for rejection are set forth in the outstanding Office Action and are not summarized here. The Examiner does, however, repeatedly stress his suggestion to include a physical limitation on “adjusting the density.” Applicants respectfully traverse this rejection.

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<sup>1</sup> The Examiner has also “emphasized that a more specific physical limitation or condition recited in the claims that distinguish two bands would obviate the basis of this rejection.” Last sentence of first paragraph on page 5. Applicants respectfully note that the claims have been amended to recite a band “having density less than 1.0792” as such a specific physical limitation

In order to establish a *prima facie* case for obviousness, the Office must establish, *inter alia*, that each and every element of the claimed invention can be found in the prior art. As mentioned above, the claimed invention is directed to an isolation method that comprises, in part, media “comprising 25% (w/v) iodixanol,” and the collection of cells from a band “having density of less than 1.0792.” Applicants respectfully submit that these limitations are “a more specific physical limitation or condition,” in accordance with the Examiner’s suggestion, which limitations are not taught or suggested in the art, particularly for the isolation of hepatic progenitor cells.

Applicants respectfully maintain that none of these references, alone or in combination, arrives at the presently claimed invention. Specifically, the combination of references, even if held to be proper, fails to teach the isolation of an enriched population of viable human liver cells comprising functional hepatocytes and hepatic stem/progenitor cells by collecting cells from a discrete band formed upon centrifugation as recited herein. Accordingly, the *prima facie* case for obvious is improperly substantiated.

Taken together and for at least these reasons, Applicants respectfully submit that a *prima facie* case for obviousness has not been established and respectfully request the withdrawal of same rejections.

### **Double patenting**

Claims 1-28 stand provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3, 4, 6-9, 12-21, 23-34 of the ‘359 application. Though the conflicting claims are not identical, they are nonetheless alleged to be patentably indistinct from each other because “the use of percoll gradients for separation of cell populations from the liver [in the two disclosures]...would render the instant set of claims obvious over the other.” Applicants respectfully traverse this rejection.

Traversal is based on the grounds that nothing in the art prior to the instant application renders obvious a process of obtaining cells enriched in human liver cells, including hepatic stem and progenitor cells, by density centrifugation in media comprising "25% (w/v) iodixanol" and selection of a "band having density less than 1.0792." For this reason and the others expounded above, the present claims are novel and non-obvious (*i.e.*, patentably distinct) in view of the '359 application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check or credit card payment form being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

By   
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Sunit Talapatra

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FOLEY & LARDNER LLP  
Customer Number: 22428  
Telephone: (202) 295-4621  
Facsimile: (202) 672-5399

Gilberto M. Villacorta, PH.D.  
Registration No. 34,038  
Sunit Talapatra, PH.D.  
Registration No. 54,482